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TITLE: Permethrin Exposure Dosimetry: Biomarkers and Modifiable Factors

PRINCIPAL INVESTIGATOR: Susan P. Proctor, DSc (USARIEM, Natick, MA)

CONTRACTING ORGANIZATION: The Henry M. Jackson Foundation for the Advancement of Military Medicine
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14. ABSTRACT

The primary aim of this project is to investigate the relationship between various modifiable factors and the absorption of permethrin as a result of wearing permethrin-treated Army Combat Uniforms (ACU-Permethrin). The research objective is to examine the effect of body weight/BMI and total energy expenditure on permethrin absorption and dose, as determined by measurement of urinary biomarkers (3PBA and cis- and trans-DCCA) levels. There are two studies involved in our project – the first is a study among Army recruits during Basic Training (Study 1) and the second involves Army National Guard Soldiers during Annual Training (Study 2). Approvals and scheduling for Study 1 are complete; data collection will proceed in Oct/Nov 2015. Study 2 data collection will occur in 2016.

15. SUBJECT TERMS
Permethrin, biomarkers, military, dose, exposure dosimetry, military, energy expenditure

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Section 1: Introduction

The primary aim of this project is to investigate the relationship between various modifiable factors and the absorption of permethrin as a result of wearing permethrin-treated Army Combat Uniforms (ACU-Permethrin). The research objective is to examine the effect of body weight/BMI and total energy expenditure on permethrin absorption and dose, as determined by measurement of urinary biomarkers (3PBA and cis- and trans-DCCA) levels. There are two studies involved in our project – the first is a study among Army recruits during Basic Training (Study 1) and the second involves Army National Guard Soldiers during Annual Training (Study 2).

Section 2: Keywords

Permethrin, biomarkers, military, dose, exposure dosimetry, military, energy expenditure

Section 3: Accomplishments

3:1 - What were the major goals of the project?

As described in the approved Statement of Work (see Table of Tasks below), the major goals during the Year 1 of this project are outlined (see highlighted section).

Year 1	***Task 1***	*Months 1-4*	-Project set up and approvals
	Task 2	*Months 4-8*	-Plan logistics for Study 1
	Task 3	*Months 4-8*	-Study 1 protocol approval
	Task 4	*Months 8-12*	-Initiate Study 1 data collection
	Task 5	*Months 10-12*	-Initiate laboratory analyses of Study 1 samples
	Task 6	*Months 10-12*	-Initiate Study 1 data management steps; integrate with USARIEM research database system
Year 2	***Task 7***	*Months 13-15*	-Prepare analytic dataset for data analyses
	Task 8	*Months 15-17*	-Initiate Study 1 data analyses to address hypotheses
	Task 9	*Months 14-20*	-Plan logistics for Study 2
	Task 10	*Months 14-20*	-Study 2 protocol approval
	Task 11	*Months 16-24*	-Report/summarize Study 1 results
	Task 12	*Months 20-24*	-Initiate Study 2 data collection
Year 3	***Task 13***	*Months 25-26*	-Initiate laboratory analyses of Study 2 samples
	Task 14	*Months 25-30*	-Initiate Study 2 data management steps
	Task 15	*Months 30-36*	-Complete Study 1 and Study 2 laboratory sample analyses
	Task 16	*Months 37-39*	-Complete integration of analytic dataset for project data analyses
	Task 17	*Months 37-39*	-Complete Study 2 data analyses to address hypotheses

Year 4	***Task 18***	*Months 39-48*	-Report/summarize Study 2 results -Prepare Project technical reports/manuscripts for publication
	Task 19	*Months 39-48*	-Provide/disseminate evidence-based guidance

3:2 - What was accomplished under these goals?

Below is a bulleted list of the projected goals and accomplishments over this study period:

TASK 1 *Project set up and (research) approvals* [**COMPLETE**]

- The research protocol was submitted to the USARIEM Office of Research Quality and Compliance and Scientific Review Committee- 17 July 2014
- The USARIEM Scientific Review Committee confirmed that that the scientific peer-review performed as part of the DHP review process was acceptable- 8 August 2014
- The protocol was approved by the USARIEM Institutional Review Board (IRB) on 4 Sep 2014 and then forwarded to HRPO for their review
- The protocol received HRPO approval 22 Oct 2014

TASK 2 *Plan logistics for Study 1 data collection* [**COMPLETE**]

- The Project Coordinator was hired in February 2015 and a Data Analyst hired in June 2015 to facilitate and administer the project data collection and analysis.
- Contract arrangements with the Centers for Disease Control and Prevention (CDC) and Pennington Biomedical Research Center (PBRC) are in place (executed agreements Apr/May2015), for the analyses of urine biomarkers of exposure (CDC) and total energy expenditure (PBRC).
- For Study 1 planning, ongoing communication with the US Army Center for Initial Military Training (CIMT) has taken place, initiating in August 2014. The PI briefed the DCG-IMT on 7 May 2015. (CIMT is responsible for coordination and approval of all research activities with BCT.)
- For Study 2 planning to take place in 2016, ongoing communication with National Guard Bureau has taken place, initiating in April 2015.
- With DCG-IMT approval (see Task 3 below), coordination with Ft. Sill POCs was initiated early June 2015 and is ongoing.
- The PI visited Ft Sill on 13 July to meet and discuss study schedules and review logistics. Study 1 dates for repeat data collection visits have been scheduled on the BCT training calendar, to initiate the week of 27 September 2015.

TASK 3 *Study 1 site approval* [**COMPLETE**]

- DCG-IMT Approval Memorandum, 1 June 2015. Approval process identified Ft. Sill as the location for Study 1.

TASKs 4, 5, & 6 *Initiate Study 1 data collection; Initiate laboratory analyses of Study 1 samples; & Initiate Study 1 data management steps* [**In PROGRESS**]

- The field study data collection for Study 1 has not been initiated. However, it has been officially scheduled to occur during the BCT course to be conducted at Ft. Sill. This delay in scheduling was the result of time required for the review and approval process at the CIMT.
- By extension, laboratory analyses of samples collected in Study 1 have not occurred but will be performed in Fall 2015.
- Data management steps, in terms of setting up the data collection instruments/surveys for Study 1 and making a plan to integration of collected data into a study database for analyses purposes, have been completed.

3:3 - What opportunities for training or professional development has the project provided?

- One Boston University School of Public Health graduate student (MPH candidate) is currently working on this project; her primary role on the project is performing data management and analytic tasks for the project.

3:4 - How were the results disseminated to communities of interest?

- Nothing to report

3:5 - What do you plan to do during the next reporting period to accomplish the goals?

- In October 2015, we will conduct Study 1 at Fort Sill, OK. Following the field data collection, urine samples will be sent to the Centers for Disease Control and Prevention (CDC) for analysis of permethrin biomarkers and to the Pennington Biomedical Research Center (PBRC) for analysis of total energy expenditure.
- Research data will be incorporated into the study database and data analysis of our Study 1 hypotheses will proceed
- As dictated in the SOW, the next reporting period will focus on completing Study 1, addressing our Study 1 hypotheses through data analyses, and planning /conducting Study 2.

Section 4: Impact

4:1 - What was the impact on the development of the principle discipline of the project?

- Nothing to report

4:2 - What was the impact on other disciplines?

- Nothing to report

4:3 - What was the impact on technology transfer?

- Nothing to report

4:4 - What was the impact on society beyond science and technology?

- Nothing to report

Section 5: Changes/Problems

5:1 - Changes in approach and reasons for change

- Nothing to report

5:2 - Actual or anticipated problems or delays and actions or plans to resolve them

- Lag in the process of identifying and for approval of a site location for Study 1 has resulted in a delay of approximately 3-4 months in completing our Year 1 ***Tasks 4, 5,*** and ***6,*** as the data must be collected before these tasks can begin. However, we are currently on target and will complete the Study 1 data collection in Nov 2015. And, in Year 2 we will be back on track with our planned task schedule for Year 2, as outlined in the approved SOW.

- The delay in completing the Year 1 Tasks will not impact in any way the progress and completion schedule of the project in the subsequent Years 2-4 SOW.

5:3 - Changes that had a significant impact on expenditures

- The delay in Study 1 site identification has caused a reduction in the amount of project funds expended over the past 6 months. However, in the Quarter 1-2 of Year 2 of the project, we anticipate the expenditure spending will be back on track in accordance with the Year 1/Year 2 planned budget spend-plan timeline.

5:4 - Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

- Nothing to report

Section 6: Products

6:1 - Publications, conference papers, and presentations

- Nothing to report

6:2 - Websites and/or Internet Sites

- Nothing to report

6:3 - Technologies or techniques

- Nothing to report

6:4 - Inventions, patent applications, and/or licenses

- Nothing to report

6:5 - Other products

- Nothing to report

Section 7: Participants and other Collaborating Organizations

7:1 - What individuals have worked on the project?

✓*Name:* Susan P. Proctor, DSc
Project Role: Principal Investigator
Nearest person-month worked: 15% of 12 person-months (1.8 person-months)
Contribution to Project: Handling all PI responsibilities for the project, including interactions with the IRB, the grantee (HJF), CIMT, Army recruit training POCs, Fort Sill, and CDC and PBRC staff.
Funding Support: Army Civilian employee

✓*Name:* Matthew M. Scarpaci, MPH
Project Role: Project Coordinator
Nearest person-month worked: 85% of 6 person-months (5.1 person-months)

Contribution to Project: Mr. Scarpaci has assumed the role of project coordination, assisting the PI in the day-to-day planning of the project, IRB tracking, HJF administrative tasks, data collection preparations, etc.

✓*Name:* Alexis Maule, MPH
Project Role: Research Associate
Nearest person-month worked: 35% of 12 person-months (3 person-months)
Contribution to Project: Ms. Maule has continued to assist the PI and project coordinator on IRB-related tasks and training additional study staff on data collection processes.
Funding Support: Boston University employee supported through USARIEM IPA

✓*Name:* Caitlin Dillon, BS
Project Role: Data Analyst
Nearest person-month worked: 50% of 1.5 months (0.75 person-months)- started June 2015
Contribution to Project: Ms. Dillon has worked on the set-up of data management tasks.

7:2 - Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

- Nothing to report

7:3 - What other organizations were involved as partners?

- Nothing additional to report

Section 8: Special Reporting Requirements

8:1 – See Quad Report

Section 9: Appendices

Quad Report

Permethrin Exposure Dosimetry: Biomarkers and modifiable factors

Log Number: 13063057 Task Area: Biomarkers to monitor for injury and disease processes

Contract #: W81XWH-14-2-0130

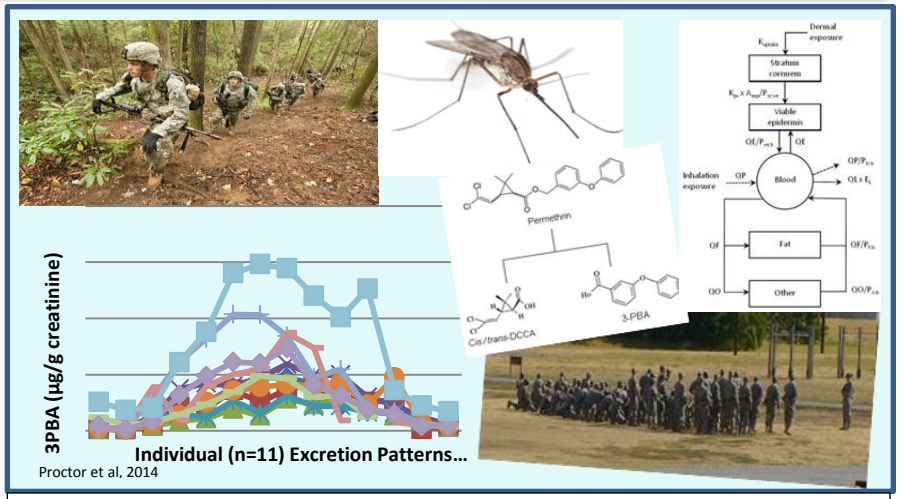
PI: Susan P. Proctor, DSc **Org:** Henry M. Jackson Foundation for the Advancement of Military Medicine (HJF) **Award Amount:** $1,861,959

Study/Product Aim(s)

- Address the influence of permethrin exposure from wearing treated uniforms (ACU-Permethrin) on human dose and monitor the potential role of exposure on health and performance for accurate policy guidance regarding potential health risk.
- The study aims to determine the modifiable factors that significantly influence human permethrin dosimetry as a result of wearing the ACU-Permethrin. Specifically, determine whether body weight/body mass index and physical activity/energy expenditure patterns influence the absorbed permethrin dose.

Approach

The project will define relationships between ACU-Permethrin wear-time scenarios among Army recruits (at Basic Training, Study 1) and Army National Guard Soldiers (during Annual Training, Study 2), urinary biomarkers of dose (3PBA, cis- and trans-DCCA), and modifiable factors (body mass index and total energy expenditure levels) to provide valid predictive models.



Accomplishments [Yr1]: Human subjects research protocol have been reviewed and approved by USARIEM IRB (#14-29H) and HRPO (#A-18378). Study 1 BCT site approved and planning steps finalized. Study staff hired. Data management plan in place.

Timeline and Cost

Activities:	Yr 1 7/14-6/15	Yr 2 7/15-6/16	Yr 3 7/16-6/17	Yr 4 7/17-6/18
Project Start-Up/Approvals				
Study 1 and Study 2 Data Collection and Sample Analysis				
Data analyses & Preparation of Manuscript & Reports				
Estimated Budget ($K)	**$718**	**$521**	**$307**	**$316**

Updated: 15 July 2015

Goals/Milestones

Yr1 Goals – Study approvals and Initiation of Study 1

- ☑ USARIEM IRB approval; HRPO approval granted Oct 2014
- ☑ Complete Study 1 site planning steps
- ☐ Initiate Study 1 data collection

Yr2 Goals– Initiate Study 1 and 2 data collection/analyses

- ☐ Initiate Study 1 data analyses
- ☐Complete Study 2 site planning steps and initiate data collection

Yr3 Goals– Complete Study 2 data collection and sample analyses

- ☐ Initiate Study 2 data analyses
- ☐ Complete Study 1 and 2 laboratory sample analyses

Yr4 Goals–Complete data analyses and manuscript(s) preparation

- ☐ Finalize data analyses and modeling
- ☐ Prepare technical reports/ manuscript(s)

Comments/Challenges/Issues/Concerns

- On target. Scheduling logistics and Budget cycle timing (see Report)

Budget Expenditure to Date:

Projected Expenditure: All of remaining Yr1 and Yr 2 funds expended in Yr2

Actual Expenditure status update as of 30 June 2015: ~$400K